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The Law of Medical Practice*

This encyclopaedic treatise (by Prof. B. Shartel and Prof. M. L. Plant, Professors of Law in the University of Michigan) has evolved out of the lectures delivered annually for the last 13 years to the senior medical students at the Medical School of the University of Michigan.

Full as the student's clinical curriculum already is, the conclusion is inescapable that adequate time will have to be found to instruct him in the hazards of actual practice in the outside world. The extent to which the doctor has become the victim of litigation makes it essential that he be instructed in the civil as well as the criminal ramifications of practising his calling.

The student's needs are more than adequately met by the chapters dealing with the *Physician's Professional Services, Compensation for Medical Care, Liability for Malpractice, Licensure of Physicians* and the *Physician's Public Duties and Liabilities.* This comprises only about half the book, however, the remaining text being specifically aimed at the actual problems of practice.

The information on licensure naturally has particular application to U.S.A. citizens, for whom the convenient gathering of data relating to the different States is in itself invaluable. But the importance to the foreign practitioner is also very considerable, as this section of the volume provides precise information about the various qualifications for admission to practice. A concise statement of the functions of the Educational Council for Foreign Medical Graduates appears at p. 205, and should greatly assist the foreign practitioner in finding his way through the maze of regulations in which the immigrant doctor may easily enough get lost.

* *The Law of Medical Practice.* By Burke Shartel, Professor of Law, University of Michigan and Marcus L. Plant, Professor of Law, University of Michigan. (1959. Pp. 431 + Index. £25). Oxford: Blackwell Scientific Publications Ltd.

It is with consternation that practitioners in many parts of the world, trained in the scientific method, will learn that

'the osteopath now can obtain a license to practice medicine in all of its branches in well over a majority of the States. . . . Under such a license an osteopath is legally authorized to do major surgery, to handle obstetrical cases, and to use and prescribe all forms of drugs, as well as to perform the traditional osteopathic manipulations.' (Pp. 216–217).

This has understandably led to strong resistance by the organized medical profession, but this disturbing conclusion is reached by the authors:

'Nevertheless on the whole the medical profession seems to us to have been winning many skirmishes but not to be winning the war . . . everything about the contest between physicians and osteopaths seems to point to the futility of the contest from the medical viewpoint, to indicate that osteopathy enjoys a better position public-relations-wise than medicine, and to suggest the desirability of reaching some form of working accord or fusion between the two professions.' (P. 218).

If this is the fate which faces the orthodox practice of scientific medicine in the U.S.A., the medical profession elsewhere should look to protect its future and the public welfare as a matter of immediate urgency.

The chapter on *The Physician's Liability for Malpractice* is a model presentation of the problems facing the conscientious practitioner. The section on proof of negligence is very clearly set out and illustrated. The description of the requirements of expert testimony includes a very apposite statement of the duty of the profession in these contentious matters, which A. Crawford Morris published in the *Journal of the American Medical Association* in 1957 (at p. 1055):

'The medical profession cannot have its cake and eat it too. This is a live and let live world. Justice is a two-way street. If the medical profession wishes to retain the safeguards of the law requiring proof of malpractice by medical testimony, it must make available to rightfully injured patients such medical proof in turn. Whatever the medical truth, patients are entitled to it too. For if the door is not unlocked by one key, it most assuredly will be by the other. Perhaps this is a problem the medical profession will have to answer for itself.'

Legal practitioners are from time to time in great difficulty about establishing proof of negligence because of the reluctance of medical practitioners to give evidence against their colleagues. While this reluctance is understandable, the medical profession must recognize that it has a duty to assist the public welfare without in any way acting unethically *vis-à-vis* their colleagues.

Students as well as experienced practitioners will find rewarding the exposition of the problems faced by the doctor as an expert witness, particularly the advice on preparation for testifying in court and the invaluable account of *Do's and Don'ts in Testifying* (at p. 345).

The final chapter comprises a general statement of the operation of the legal system and constitutes a valuable introduction and guide to what is often a confusing maze to the layman.

There can be little doubt that the authors have produced a major, if not a definitive contribution to our forensic literature.

Biochemical Changes In Cadaver Sera

In Fatal Acute Heart Attacks

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Recently biochemical methods based on release of enzymes from necrotic cells have been added to electrocardiographic examination as means of confirming clinical diagnosis of myocardial necrosis. Not only have these rendered differentiation between organic change and functional coronary insufficiency more precise, but they can also be recognized before the end of the period which must elapse for pathological changes to be recognized *post mortem;* indeed, about one half of attacks of fatal cardiac ischaemia show no recent morbid anatomical changes. As the blood can rarely be examined during the course of an attack which terminates within a few hours, enzyme assays have been made on cadaver sera to determine whether this method can demonstrate occult necrosis in such cases.

Two forms of transaminase and lactic dehydrogenase have been studied in detail. To assist interpretation, serum phosphatases and amylase and C-reactive protein have also been estimated and accumulation of other organic substances probably related to autolysis has been observed.

Materials and Methods

About 800 sera from 785 corpses have been examined. Collection of adequate satisfactory samples is most easily carried out by elevation of the arm after the axillary bundle has been severed; commonly 10–30 ml. then flows from the cut end. The mean temperature of the air and of the mortuary refrigerator were recorded and the mean temperature to which the body had been exposed calculated. Serial samples collected by syringe proved quite unsatisfactory. Grossly hemolysed sera, about 1 in 8, were discarded and many of the others were passed through a centrifugal Hemming's filter. Sera came from 6 mortuaries; 32 samples from one of these showed a large systematic difference, probably due to delay in transportation, and these were discarded. Necropsies and diagnoses were made by 4 pathologists over the past 3 years.

C-reactive protein,[1] amylase[7] and lactic dehydrogenase[10] were estimated by standard methods. In the phosphatase methods[8] the blank values are due to Folin and Ciocalteau-reacting phenolic substances in the test serum. The

difference between the mean of the acid and alkaline serum blanks and the reagent blank was coverted into μgm.-equivalents of phenol (μgm. eq.) by dividing by the extinction of the standard and multiplying by 300. The alkaline blanks were consistently about 10% higher than the acid blanks. Haemoglobin was estimated spectroscopically and arbitrarily graded; the value of one unit of grading was assessed by additional chemical estimations on 44 of the sera by Wu's method as modified by Bing and Baker[2] and found to be approximately 100 mg. (mean value 100.9 mg. per 100 ml.).

Transaminase activity was estimated in 3 ways. In 53 sera a minor modification of the laborious *chromatographic method* of Karmen, Wroblewski and LaDue[6] with quantitative ninhydrin colour development by the Troll and Cannan procedure[9] was employed. This method was studied in considerable detail and 20 living subjects were also examined. Enzyme activity was linearly related both to time and amount of enzyme until equilibrium was reached at about 16.0 μM of accumulated glutamic acid in the 1.2 ml. of reaction mixture. This imposed a limit of activity of 5.0 μM per ml. per hr. on successful estimation of undiluted sera in 60 minutes. Most post-mortem sera were considerably more active than this and all were outside the normal range. Two-dimensional chromatography of a glumatic-oxalacetic equilibrium mixture incubated for 17 hours revealed several ninhydrin-reacting substances not taking part in the simple reaction.

Table 1: Distribution of Ninhydrin-Reacting Substances in Chromatograms of Equilibrium Mixtures of Serum, Aspartic and Alpha-Oxoglutaric Acid

Substance	*Relative Intensity of Spot*
Aspartic acid	Completely Removed
Glutamic acid	4
Glycine	1
?	Trace
Alanine	3
Histidine or lysine	1
Valine	Trace
??	Trace

Table 1 shows these substances reading in the direction of flow along the phenol axis of a phenol/butanol-acetic acid chromatogram. Their appearance in non-equilibrium test mixtures was variable; the mean times after death of 25 sera in the chromatograms from which the alanine spot was recorded was 33.2 hours and in 37 in which its absence was marked 33.9 hours.

Two hundred and fifty-one estimations were made by the *colorimetric procedure* of Frankel and Reitman[4] using commercial (Sigma Chemical Co. Ltd., St. Louis, Mo., U.S.A.) reagents. Separate calibrations were made for glutamic-oxalacetic transaminase (SGOT) and for glutamic-pyruvic transaminase (SGPT). The blanks values varied considerably. In 10 consecutive batches with an Ilford 604 filter they ranged from E 0.14 to E 0.23

for SGOT and E 0.17 to E 0.24 for SGPT with means of E 0.168 and E 0.127 respectively. Accordingly corrections were applied. In the middle range diluted sera invariably indicate a higher activity than do neat sera; in 5 duplicates at dilutions of 1 : 1 and 1 : 10 the latter indicated a mean activity almost exactly 3 times as high. The value of one unit (SFu), calculated from the molecular extinction of diphosphopyridine nucleotide which forms the basis of the spectrophotometric assay of Karmen *et al.*[6] appears to 0.029 μM per ml. per hr. This factor has been used to convert SFu into data comparable to those from the other two methods.

A further 233 sera were estimated by a modification of the *spectrophotometric* Cammarata and Cohen method[3] which is especially suited to high activity preparations such as these. Absorption of ultra-violet light by oxalacetic acid at 270 mμ is enhanced by borate (Greenwood and Greenbaum)[5] to a point at which its development can be followed directly after deproteinization. The following procedure has probably not previously been used on human material.

0.2 ml. of each serum is placed in each of 2 tubes (3 x ½ in.) in a water bath and allowed to reach 37° C. The substrate is an 0.025 M solution of aspartic and of *alpha*-oxoglutaric acids in 0.06 M phosphate buffer at pH 7.6; 0.8 ml. of this, also at 37° C., is added to the test tube to start the reaction. After 10 minutes 0.8 ml. is also added to the control to be followed immediately by 0.5 ml. of 20% trichloracetic acid to both tubes. These are at once centrifuged. Without delay 1.0 ml. of supernatant fluid is added to 3.3 ml. of neutralizing buffer solution (260 ml. 0.5 M boric acid and 170 ml. N NaOH in 1 L). In 15–30 minutes the difference between test and control tubes is read at 270 mμ dE $\frac{1 \text{ cm.}}{270}$ 0.01 represents an activity of 0.67 μM per ml. per hr.

The ultra-violet absorbing power of the control (serum blank), which is essentially a 1 : 30 dilution of deproteinized serum in borate buffer at pH 10, was also recorded.

Results

The grouping of the cases is shown in Table 2 which also shows results of *C-reactive protein* estimation on 386 of them. In the enzyme analyses the sub-groups were not employed, but the differences confirm the essential soundness of the major divisions. Further confirmation has been derived from numerous analyses of serum lipids which will be published elsewhere. No evidence that autolytic changes affected the presence of C-reactive protein was obtained.

Very high *transaminase* activities were encountered, up to a maximum of about 200 times mean normal (case 117, 37 hours *post mortem* 3,500 Sigma Frankel units; Case 330, 30 hours 63 μM per ml. per hr. by chromatography; case 108, 29 hours, 99.0 μM per ml. per hr. by the method here reported). Serial estimations have confirmed that the enzyme is stable in these solutions of high protein content over the relevant storage period. Arm rather than heart blood was chosen since the latter was not uniform,

Table 2: Distribution of the Cases, the Results of C-Reactive Protein Estimations and Some of the Transaminase Results

Group and Diagnosis	*C-Reactive Protein*		*Transaminase by Sigma Method*			*Transaminase by All 3 Methods*
	No. of Cases	*Per Cent. Positive*	*No. of Cases*	*Corrected Mean Difference*	$\frac{SGOT}{SGPT}$	*No. of Cases*
1. Coronary occlusions without fibrosis, necrosis or thrombosis	50	24	34	1·1	0·8	93
2. Myocardial fibrosis without recent changes	28	32	20	0·5	1·3	32
3. Myocardial necrosis	56	61	31	—3·0	0·8	70
4. Coronary thrombi with no record of necrosis	22	45	14	1·4	0·4	39
5. Non-coronary heart disease:	64	80	37	1·3	1·0	65
(*a*) Valvular and congenital ..	(16)	(44)				
(*b*) Vascular and hypertensive	(31)	(57)				
(*c*) Pulmonary emboli ..	(13)	(92)				
(*d*) Cor pulmonale (*Total*)	(4)	(100)				
6. Bronchopneumonia	45	82	21	—2·6	0·8	60
7. Other chest conditions:	20	80	16	—0·9	0·8	18
(*a*) Influenza						
i. Infected ..	(4)	(100)				
ii. Uninfected..	(4)	(25)				
(*b*) Lobar pneumonia ..	(6)	(100)				
(*c*) Chronic pulmonary fibrosis	(6)	(50)				
(*d*) Tuberculosis ..	(4)	(100)				
(*Total*)						
8. Immediate traumatic deaths	19	16	13	2·7	6·0	27
9. Poisonings ..	20	30	15	1·4	0·6	35
10. Intracranial haemorrhages	15	40	9	1·1	0·7	26
11. Infants (under 1 year)	15	7	5	7·7	0·6	6
12. Neoplasm ..	34	79	19	—0·4	1·2	40
13. Miscellaneous lesions	26	98	17	3·0	1·4	26
	386					537

was more haemolysed and gave higher and more irregular transaminase values. In 7 pairs of sera the heart specimens contained about 2.5 times as much haemoglobin. In 9 pairs the transaminase level was from 1.3 to 8.5 times higher in the heart and in the tenth pair it was 42 times higher.

An analysis to discover any possible biassing effect due to conditions other than the cause of death was made on the results of the 251 sera uniformly analysed by the Sigma procedure. To simplify working, the units were converted into common logarithms (log SGOT), a procedure suggested by the log-normal distribution of the values. The mean ages in all the groups was fairly uniform apart from the infants and the traumatic group (39 years). Males predominate in all groups except poisoning, cerebral haemorrhage and infants. The different pathologists appear to have used comparable diagnostic criteria. No group predominated at any of the mortuaries except cancer, most of which cases were examined at the major hospital mortuary included. Oddly enough there was no marked disproportion in any of the groups in the warmer months; in any event in this year of the survey warm weather was quite uncommon. The time elapsing between death and necropsy was correlated with transaminase activity in the samples, the correlation coefficient (r) of the mean time for successive increments of activity (which were grouped until each point represented at least 6 samples) being 0.66. With log SGOT as the independent variable the relationship is represented by:

$$\log \text{SGOT} = 10.2 + 0.47 \text{ (time in hours)}.$$

The single mean value corresponding to very low activities, which will be shown to occur after both long and short time intervals, is largely responsible for the incomplete correlation; if it is omitted the S.D. of log SGOT falls from 7.14 to 5.43.

None of the other parameters provided significant correlations to assist interpretation. The mean temperature to which the bodies were exposed actually gives a negative regression coefficient (b) but correlation is poor and ($r = -0.44$) and the measure of certainty is only 0.19. The formula is

$$\log \text{SGOT} = 41 - 1.37 \text{ (mean temperature in C°.)}.$$

For air temperature the formula is

$$\log \text{SGOT} = 37.4 - 0.81 \text{ (mean air temperature on day of death in C°.)}$$

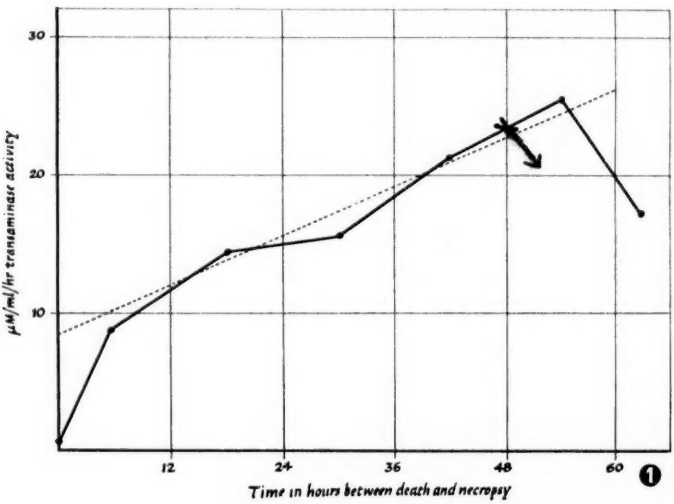
and $r = 0.35$. An attempt to combine these two sets of data into a single index for the 3 parameters gave $r = 0.53$ and $b = 3.82$, a less close relationship than that for time alone.

Further analyses were confined to the influence of cause of death and of time elapsing thereafter. The mean activity in successive 12-hour periods in the 3 series estimated by entirely different methods was very similar, with the sole exception of the small group of 5 chromatographic estimations performed in the first 12 hours (21.4 μM per ml. per hr. against 8.0 and

8.8 μM per ml. per hr.). Fig. 1 shows the trend of enzyme accumulation derived from all 537 estimations and indicates that it occurs in 3 phases. After an initial rapid rise the slope of the main line remains constant until 60 hours, after which there is a fall. Two necropsies were made in the second hour and the average activity in them was 1.7 μM per ml. per hr. while 4 in the third hour averaged 5.1 μM per ml. per hr. The mean activities in the second, third and fourth 3-hour periods were 10.7, 12.3 and 10.9 μM per ml. per hr. The initial rise is not therefore actually agonal but the main slope is established by about 3 to 4 hours after death. The correlation between all the individual values of time and activity is not very close ($r=0.29$) but does reach conventional limits of significance (s.e.$=0.045$). The formula relating them is

μM per ml. per hr. transaminase activity $= 9.44 + 0.316$ (time after death in hours).

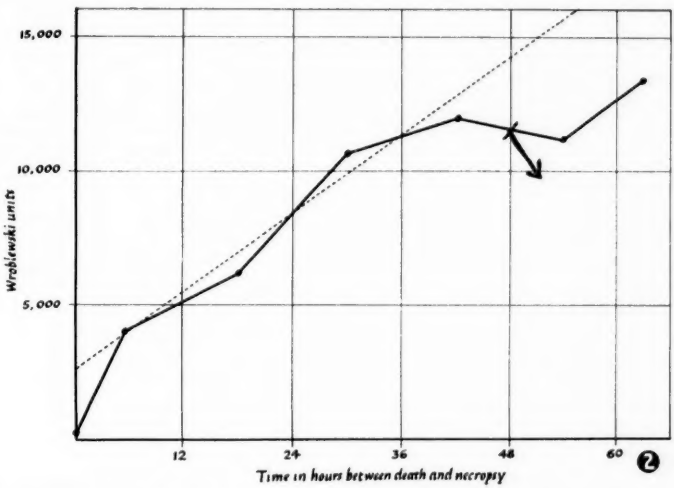
The individual disease groups were then examined. In the Sigma series the mean observed value in each was corrected for the difference between its mean time and the mean time of the whole series (30.3 hours) by the formula relating time to log SGOT above. Only the myocardial necrosis cases and the infants were apparently different (Table 2, column 4) and for them the significance of the difference between their mean activity and that of the remainder corrected to the same mean time, was calculated. The probability that the corrected mean activities were not different was 0.045 in the myocardial necrosis cases and 0.001 in the small group of infants. For this latter reason no further sera were collected from infants. The probability that the coronary occlusion group did not differ was only 0.032 and that it did not differ from the necrosis group 0.08.



1

The larger numbers of the full series enabled graphs representing enzyme accumulation in each group to be compared. Within the first 48 hours none appeared to depart significantly from the mean line. The two groups of recent organic ischaemic heart disease (3 and 4), however, both showed an earlier fall than the remainder and this effect was confirmed by examining separately all 3 series. The difference between the mean of the values for those 2 groups combined in the 49–60 hour period and the mean of all the other values in that period was 16.2 μM per ml. per hr. and was highly significant ($r = 3.36$ for 61 d.o.f.; $p < 0.01$). No other significant differences were discovered.

SGOT : SGPT ratios were estimated in 70 subjects; the results are given in column 5 Table 1.



Accumulation of *lactic dehydrogenase* was found to follow a very similar pattern over the first 60 hours (Fig. 2) and for this period the correlation of the individual values was slightly better than that for transaminase ($r = 0.32$; S.E. 0.06). The formula relating them is:

Wroblewski units of lactic dehydrogenase/1000 = 2.69 + 0.24 (time after death in hours).

After 60 hours the serum activity does not fall during the whole period during which necropsies were done, the mean values of the periods 61–72 hours, 73–84 hours and 85–96 hours being 14,000, 13,100 and 13,700 W.U. per ml. per hr. Separate curves for the different groups did not present any significant differences, Group 1 in particular following the mean line almost exactly. The means of the combined groups 3 and 4 and the remainder in the 48 and 60 hour period were 13,000 and 13,600 respectively.

There was a fairly good correlation between these 2 enzymes in 150 individual sera (r = 0.84, S.E. 0.082). The formula relating them is
μM per ml. per hr. SGOT = 4.4 + 0.86 x Wroblewski units lactic dehydrogenase/1000.

Accumulations of acid and alkaline phosphatase and amylase are shown in Table 3. The trends are not as clear as with the larger series of the other enzymes but the changes have a similar pattern. There are two main differences: the rises are much smaller (highest values: alkaline phosphatase 216 KAu per 100 ml. = 34 times normal mean; acid phosphatase 111 KAu per 100 ml. = x 55; amylase 576 units = x 6) and all 3 enzymes show a fall after only 48 hours. In the few cases in which it was examined the distribution throughout the body appeared to be much more uniform, e.g. case 117: arm blood acid phosphatase, 10 units alkaline phosphatase 14 units; right atrial blood 10 and 19 units.

Table 3: Accumulation of Enzymes in Cadaver Sera

Time Periods Between Death and Necropsy (In Hours)	2—12	13—24	25—36	37—48	49—60	>60
			Mean Values			
Glutamic-oxalacetic transaminase in μM per ml. per hr. All 3 Methods	9·2	14·6	15·8	21·5	25·8	17·1
Normal mean = 0·5 μM per ml. per hr.						
No. of tests	75	138	135	83	62	44
Lactic dehydrogenase in Wroblewski units/1,000 ..	4·1	6·3	10·7	12·0	11·2	13·6
Normal mean approx. 250μ						
No. of tests	45	80	66	43	30	26
Acid phosphatase in King-Armstrong units	10	28	19	41	30	30
Normal mean 2 units						
No. of tests	14	15	12	9	2	1
Alkaline phosphatase in King-Armstrong units	15	30	39	73	49	24
Normal mean 7 units						
No. of tests	14	15	10	7	2	1
Amylase in Somogyi units ..	350	310	170	370	202	—
Normal mean 100 units						
No. of tests	4	11	6	5	2	0

Accumulation of 3 non-enzymic organic substances was also followed (Table 4). *Haemoglobin* rose rapidly in the first 12 hours followed by slow accumulation up to 48 hours. The mean value for the 5th 12-hour period falls slightly but the mean for the times above this is again higher. The transaminase activities of 8 specimens of fresh whole blood, diluted 1 : 1000 with distilled water, lay between 5 and 15 SFu per ml. for haemoglobin

content of 6–16 mg. per 100 ml. The relationship was roughly linear. The activity of plasma is negligible at this dilution and there was thus a mean activity of 133 SFu per ml. for each 100 mg. per 100 ml. of haemoglobin. The high activities of post-mortem sera cannot therefore be attributed to their haemoglobin content.

Table 4: Accumulation of Non-Enzyme Substances in Cadaver Sera

Time Periods Between Death and Necropsy (In Hours)	*0—12*	*12—24*	*24—36*	*36—48*	*48—60*	*>60*
			Mean Values			
Hemoglobin mg. per 100 ml. by visual spectroscopic assessment	42	66	60	70	43	87
Normal mean 2 mg. %						
No. of tests	27	32	48	20	20	8
Phenolic substances μgm. equivalents per 100 ml.	177	250	280	461	331	600
Normal average value = 110 μgm. per 100 ml.						
No. of tests	13	15	11	7	2	1
Opacity of deproteinized serum to ultra-violet light $E_{270}^{1\,cm.}$ (*see text*)	0·54	0·65	0·78	0·87	0·75	0·84
Normal value approx. = 0·1						
No. of tests	20	39	33	26	19	19

Phenolic substances show the same trend as the haemoglobin results although the rate of accumulation is slower in the first 12 hours and more rapid thereafter. A fall in the mean level in the 5th 12-hour period is again seen. The highest value encountered in the first 12 hours was 345 μgm. eq. and 485 μgm. eq. in the second 12 hours.

The *serum opacity to ultraviolet light at* 270 μ showed an almost identical behaviour, the maxima encountered in the first two 12-hour periods being $E_{270}^{1\,cm.} = 0.8$ and 1.05.

Because of the complex nature of these curves no correlations have been calculated.

The data in 34 cases dying up to 60 hours before necropsy and in which estimates of transaminase, lactic dehydrogenase and ultra-violet opacity of the serum were all made referred to the accumulation lines of these substances. The mean of the 3 time intervals so indicated was compared with the actual time after death at which the serum was collected. The mean difference was 15 hours with a S.D. of 13 hours on a mean time of 30 hours.

Discussion

This investigation shows that some quite refined clinico-pathological tests can be carried out on cadaver sera, but it also shows that interpretation of the results is much more complex than in the living subject. A large number of results is necessary before a pattern of accumulation can be discerned, but when there are sufficient data the effects of disease can sometimes be indicated with a high degree of probability.

Considerable effort was made to confirm that the enzyme mainly studied was in fact glutamic-oxalacetic transaminase. Some of the results were compared with those of a similar test for glutamic-pyruvic transaminase on the same serum; this was in fact found to behave in a similar fashion—and thus was of no value in differentiating enzyme of cardiac origin from that arising in other organs such as the liver. Chromatography showed that transamination was occurring in the tests and enough sera were examined to demonstate that this method gave results almost identical with indirect estimations. Formation of other substances did not apparently affect transamination. Two different and separate ways of following the non-nitrogenous end products of the reactions were employed and again gave almost identical results. Finally a calculation was made comparing the highest activities encountered with those obtained by Vernon[11] on a purified preparation of pig's heart transaminase which had been concentrated 70 times. As little as 0.04 g. of enzyme protein per 100 ml. cadaver serum could account for these activities. It thus appears that, despite high and variable blank values in all 3 methods, the measurements made probably are of serum transaminase activity.

Characteristically all the substances studied accumulated in cadaver sera in 3 phases with the passage of time after death. Firstly a rapid rise occurs within a few hours to levels well outside the normal range in living subjects. Next a slower, progressive and usually linear increase occurs over the next 2 or 3 days, and subsequently there is a fall. After this time there is more variation in the behaviour of the individual substances and the changes due to disease may usefully be sought for in this period. The 5 enzymes studied all fell off, but the time of peak activity was different. Both forms of phosphatase and amylase were less active in the fifth 12-hour period than they were between 36 and 48 hours, whereas transaminase showed peak activity in the fifth period and lactic dehydrogenase even later still, probably on the fourth day. These data presumably reflect the stability of the proteins of which these enzymes are composed. The 3 non-enzymic substances studied, while also at a peak level at about 48 hours, showed a purely temporary fall during the next period, rising to higher levels thereafter. There was no evidence of a final fall in the cases examined. This temporary fall was only of the order of one third of the

mean level in the preceding period, but as it was seen in all 3 substances it is probably a real phenomenon and perhaps related to breakdown of cell walls that occurs at about this time.

The behaviour of these non-enzymic substances was studied in the hope that they might enable an index to be derived from which enzyme activities could be corrected for decay factors. Since it differed from that of the enzymes they were not found to be helpful for this purpose, nor were they much more useful when used by themselves to assess time of death. Occurrence of values above the maxima given above could with some certainty place a time of death as more than 12 or more than 24 hours previously, but in this series in only 15 of 205 cases could the data be of assistance.

Numerous other attempts were made to derive a more accurate method of prediction of time of death by combining the data in various ways, but none showed any real promise. In view of the expense and complexity of some of these investigations it was concluded that there was no reasonable probability that further exploration along these lines would be profitable.

Application of the enzymic data to the initial problem has produced a clear but negative answer. The cases were grouped by morbid anatomical criteria without reference to possible aetiological relationships between them and the estimations of C-reactive protein gave some logical confirmation that this was sound. From the separate group accumulation curves it is possible to show beyond reasonable doubt that transaminase activities in persons who have died from myocardial necrosis or coronary thrombosis, the two conditions in which recognizable changes are seen in the sera of clinical cases, differ from those in persons who have not died from heart disease. The activity of the serum falls off sooner in this group than in the remainder and this is presumably explained by ante-mortem destruction of some enzyme, which has leaked from myocardium to serum in the interval between necrosis and death. The group of coronary occlusion cases, on the other hand, behave in the same way as all the others and so present no biochemical evidence of necrosis. The data from the Sigma series of estimations support this interpretation; here again a difference between the myocardial necrosis cases and the remainder just reaches conventional levels of significance whereas the coronary occlusion cases show no difference. It may therefore be concluded that, on these criteria, subjects who have died from simple coronary occlusion more closely resemble those who have not died cardiac deaths than they do those who have died from organic ischaemic heart disease demonstrable by recent organic change.

Summary

Estimations of transaminase, lactic dehydrogenase, phosphatase and amylase activity and content of haemoglobin, phenolic substances and opacity to

ultra-violet light of deproteinized solutions have been made on some of 800 sera obtained from 785 cadavers. Glutamic-oxalacetic transaminase was estimated on 537 arm blood samples collected between 2 and 96 hours *post mortem*. All these substances were found to accumulate in the serum after death, at first rapidly for a few hours and then more slowly for 2–3 days. Enzyme activities fell off thereafter but the inactive substances, after a fall on the third day, again rose progressively. C-reactive protein was also estimated to assist in grouping the cases but no evidence that it varied with time after death was found.

Significant differences from the common pattern of transaminase activity were demonstrated in sera from cadavers showing evidence of myocardial necrosis. Cases dying from coronary occlusion without evidence of recent organic change more closely resembled the control series than those with myocardial necrosis or coronary thrombosis. No significant differences in lactic dehydrogenase activity attributable to the cause of death were found in these cadaver sera.

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Penetrating Wounds of the Aorta Ascendens and of the Heart

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History

Penetrating wounds of heart and of great blood vessels have often been the subject of publications by various authors. All of them agree that wounds of heart are fatal, but that death does not necessarily take place instantly. It may be delayed for a few hours, days or even weeks. The most frequent penetrating wounds of heart are those due to knives. They are located mostly in the right ventricle, as this forms the greatest part of the anterior cardiac surface. Thereafter, according to frequency, follow stab wounds of the left ventricle, the aorta, the pulmonary artery, the auricle and the vena cava.

The wounds of the auricles and of the great blood vessels are generally rapidly fatal. Stab wounds in the left ventricle do not result always in sudden death. This may be due to very thick wall of the left ventricle, which is the case particularly when the wound is given obliquely; when the heart contracts the wound also contracts. Therefore, in such cases death may occur only after a few days. Stab wounds in the right ventricular region more often result in death than those involving the left ventricle; also wounds of the base of heart may more often lead to death, in consequence of rapid bleeding, than those caused to the apex of the heart, where the blood can flow out freely into the pleural cavities, so that no pressure on the heart occurs, and there is no disturbance of its function, as is the case with cardiac tamponade.

As little as 250 c.c. of blood can cause tamponade. It always happens when the blood in the pericardial sac is accumulating more rapidly than it can be expelled through the pericardial wound.

Increased intrapericardial pressure then arises, and collapse of great veins. According to Moritz[1] the so-called 'Trinity of acute pressure' appears, i.e.

1. Increase of venous pressure;
2. Decrease of arterial pressure;
3. Gradual cessation of heart function.

The time of accumulation of the blood in the pericardiac sac may vary from a few seconds to a few hours, on which depends the duration of life after the injury. Moritz considers that with sudden blood accumulation in percardiac sac it is not possible for that accumulation to be in excess of 300 to 400 c.c. of blood, in distinction from the cases of slow accumulation

of fluid in some diseases, when hydropericardium appears. Then it is possible to find even about 1,000 c.c. of fluid. Adanja[2] and others consider that the quantity may reach 2–3 litres.

In cases when the blood flows freely into the pleural cavities, death results from haemorrhage, the duration of life being dependent upon the size of the wound. If the death occurs quickly, immediately after the heart wound, then the cause is most frequently a reflex shock or disturbances in the atrio-ventricular node or in the conducting system. In later stages death may result after a penetrating wound of the heart from pericarditis and mediastinitis (as blood is an excellent nutrient medium for bacteria) and from cerebral embolism.

Penetrating wounds of the auricle, the pulmonary artery, the aorta, and the coronary artery are the wounds which most quickly lead to death, as in case of these injuries the bleeding is fast and profuse.

Emara and Soliman[3] cite Taylor's case in which a boy who had been stabbed in the heart, did not die for 8 days. Death was due to cardiac tamponade. Oliver and Sansom elaborated the materials of 29 penetrating heart wounds, among which only 2 cases resulted in death within 24 hours; while in other cases death occurred only within a period of 4–28 days. Kerr[4] pointed out 3 cases published in Taylor's *Medical Jurisprudence*.

The first case was a man who discharged a bullet into his heart twice; with one bullet he injured the right ventricle, and with the other the left ventricle. He did not die until 1½ hours later.

The second case was a man who had been stabbed in the left ventricle, after which he had run 18 yards and was still alive 6 hours thereafter.

The third case was a stab with a stylet. The wound was in the left ventricle, and the man died only after 24 days.

Harris (cited by Kerr) describes a case of a stab into the intrapericardiac part of the upper vena cava where the victim continued to run, jumped over a fence and traversed 30 yards before he collapsed and died.

Ranasinghe[4] describes an interesting case of a young man with several self-inflicted wounds of his chest; after that he ran 200 yards and then he swooned. A short time before he asked for a drink; he died 23 hours after the wound. The stab wound passed through the pericardium, the anterior wall of the right ventricle, the base of interventricular septum and through the left ventricle. The great blood vessels and the coronary artery were not injured. Microscopic examination of the brain revealed cerebral embolism. The cause of death was cardiac tamponade.

Gonzales and others[6] noted a similar case of mural thrombosis and of cerebral embolism, which appeared 24 hours after the injury. Glaister[7] points to a case of a young man who, after the heart injury ran after the attacker for 40–50 yards and only then collapsed.

Davidson and Fiddes[8] mention a case of an adolescent who had been stabbed into the right ventricle, and who proceeded 600 yards in 20 minutes before he collapsed. He died 1½ hours after receiving the wound.

Similar cases are also described by Glaister,[7] Greval,[9] Kerr,[4] Smith and Simpson,[10] Mann and Brend[11] and Muller.[12] Mann and Brend[11] describe a man who died 4 days after the stab in the heart, and during that time he lifted heavy burdens. Gonzales records a case where the victim stabbed in the heart was running, crossed a street and then went up 2 stairs to his dwelling, closed himself in the bathroom and died.

Tesar[13] cites the case of Kratter who describes the case of a policeman stabbed in the right side of the heart. After that he killed his attacker before he himself died.

In the same work is mentioned a case described by Slavik (cited by Tesar). A 32-year-old man came home drunk. During a quarrel his wife stabbed him in the heart region. He fainted, and when he regained consciousness he fell asleep and slept until next morning. Next day he walked the whole day. On the third day he was on a trip and was again drunk, came to blows, and in the afternoon beat his wife. In the evening he fell asleep. During the same night at 2 a.m. he had a sexual intercourse with his wife and on that occasion he died. The death occurred due to cardiac tamponade. At the site of the stab wound in the right ventricle the thrombus which had formed, was destroyed.

A similar case was pointed out by Hajek (cited by Tesar) where the stab wound caught the pericardium and the left heart muscle and death came only on the tenth day.

Cosman *et al.*[14] present a case of a penetrating wound in the right auricle; here secondary recurrent haemorrhage appeared. This is not known in literature.

However, Perkins and Elchos[15] and also Beattie and Greer[16] point to cases of successful recovery after surgical intervention of the injured aorta. The first such case was noted by Džanelidze in 1922 in Russia (cited by Perkins and Elchos) where there was a large stab wound in the aorta, immediately behind the valves.

Survey of the Cases

Two interesting cases are presented, one involving the aorta and the other the heart.

Case 1

A man of 25 years of age was stabbed by his father in the chest during a quarrel. The time was about 4 p.m.. He had immediately been transported by wagon to the hospital, a distance of about 20 kilometres. He was conscious on arrival, pulse 80 per minute and full; blood pressure 115/75 mm. Hg.

On the left side of the chest there was a stab wound 2 cm. long, obliquely placed, which was not bleeding. He received penicillin, strepto-

mycin and a transfusion of blood. He felt well, was conscious, and speaking. About 11 p.m. on the same day he began to complain of pain in the region of the wound; he became restless, but the pulse was regular. Suddenly, at 5 minutes after midnight, he lost his pulse, was dripping with cold

sweat and became cyanotic. He was given oxygen, but the cyanosis became more and more progressive, the respiration irregular and he died at 12.30 a.m. The diagnosis was: vulnus ictum thoracis, shock, ?cardiac tamponade.

Autopsy showed that at the sixth left rib there was an obliquely placed, fresh surgical incision. The soft tissues of the anterior mediastinum were diffusely suffused with blood for 2 cm., and covered with about 200 c.c. of clotted blood. The pericardium was empty, and at the apex there was a stab wound about 28 mm. long. In the left thorax there was about 500 c.c. of liquid blood. One finger below the heart base in the region of right ventricle there was an obliquely placed stab wound 15 mm. long with flat edges. The track of the wound continued through the upper part of the interventricular septum, obliquely in an upper direction through the anterior tricuspid valve where there was a stab wound 1 cm. long; then it continued through the bulbus of the aorta about 0.5 cm. above its origin. The wound of aorta was 15 mm. long. On the septal valve of the aorta there was a stab wound in continuation of the aorta wound, and the wound ended on the anterior cusp of the mitral valve in the form of a small surface excoriation near the attachment (Figs. 1–3).

This patient received a punctured pericardial wound of the right ventricle and the aorta, after which he proceeded 20 kilometres by wagon, always being fully conscious, with a normal blood pressure and pulse, and he died 8½ hours after the injury.

Case 2

A man of 36 years had been shot on the back by a gun. He walked 5 steps forward, turned round and fell dead.

At autopsy the entrance of the gun-shot wound on the back under the left shoulder blade was 1 cm. in diameter, and 2 exit wounds were present in the region of the right clavicle. A circular interruption of the aorta was found in the form of lobule, about 3 cm. over the valve of aorta. In the pericardium there were about 20 c.c. of liquid blood and in the right pleural cavity only a few c.c. of blood. In view of the extensive nature of the injuries it was possible to conclude that the wound was caused by the so-called 'dum-dum' projectile, producing an 'explosive' wound.

Discussion

On the basis of literature reviewed and of examples described here, it is possible to conclude that injuries of the heart and the aorta do not necessarily lead to instant death. On the contrary, it is important to remember that persons with heart injuries are in a position to execute some operations which are often complicated and difficult, before the injuries cause death. The period of survival varies and depends on the site of the wound in the heart, its direction and, particularly, on the quantity of blood lost.

In Case 1 a stab wound involved the right ventricle of the heart and the ascending aorta; and the injured person lived for 8½ hours. The normal,

regular pulse indicated that the conducting system was not injured, and there was no greater bleeding, particularly in the pericardial cavity, because the stab in the heart was very obliquely placed, so that the sides of the wound could become apposed to each other during contraction of the heart, in this way obviating profuse bleeding.

The bleeding into the anterior mediastinum could postpone death until compression from outside on the great veins was great enough to lead to death.

The mechanism of death was the same as in cardiac tamponade, i.e. mechanical prevention of function of the heart.

It is very probable that the coagulum of blood in the mediastinum plastered up the opening in the ascending aorta, so that it was impossible to create quick drop of arterial pressure. In this way it is possible to explain such long survival after a penetrating wound of the ascending aorta.

Case 2 is certainly very instructive, as entire interruption of the ascending aorta occurred, and the injured person nevertheless succeeded in taking a few steps.

The possibility of movement and execution of some operations after stabs in the heart, less so in the aorta, is very limited; yet we must allow the possibility that every and any kind of action during any period in the cases of those injured in the heart and aorta is possible.

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Quantitative Determinations of Ethanol

Besides Other Volatile Substances in Blood and Other Body Liquids

By Gas Chromatography

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Abstract

In the present paper the use of gas chromatography for rapid and specific determination of alcohol in blood is reported. Using hydrophilic stationary liquids (diglycerol, carbowax) and a 2-column system, it was possible to avoid the preliminary conditioning of the blood; by introducing inner standards of volatile substances (N-butanol or methyl ethyl ketone) which were added to the blood samples, the necessity of accurate dosing of the injected samples could be avoided. Measurements were executed on a thermal conductivity apparatus and also with a Czechoslovak chromatograph which is fitted with a ionization detector. By refluxing water damp (thermal conductivity detection) higher speed of the analysis was achieved; application of an ionization detector allowed qualitative differentiation of the remaining substances and treatment of smaller samples of blood, urea or other liquids of the human body which are subjected to medical or forensic examinations.

Studies of the average error and determinations of the conversion factor were made. The obtained sensitivity is 0.1 ‰, the stated relative error was maximum 5% relative for the limit of 0.8–1.9‰ alcohol, using 0.01 ml. samples (thermal conductivity) or about 0.02 ml. samples (ionization detection). The elution interval of the other alcohols and volatile substances in blood was determined.

In recent years increased attention has been given to questions concerning the determination of alcohol in blood. This is a consequence, on the one hand, of the more severe laws introduced to maintain security of traffic and, on the other hand, a consequence of the imperfections in the present analytical methods. The currently used method of Widmark[1] and its numerous modifications determine besides alcohol also all reductive volatile substances in blood. It is interesting to note that Widmark's method (which was derived from the previous method of Nicloux) has been used for 3 decades all over the world. Only during recent years in Germany and Switzerland have control determinations of alcohol by some other method been required. But these methods also do not meet the requirements for the specific determination of methyl alcohol.

The completion of Widmark's method by interferometric determinations was connected with some technical difficulties.[2] The new method of Vidice[3] based on the

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reduction of orange vanadium oxide to blue vanadyl sulphate is, we admit, more precise and suitable than the oxidation by dichromate, but it is lacking in specificity, too.

The method of Schifferli[4] based on the pyrogenic dehydration of ethyl alcohol to ethylene requires, on the one hand, 10 ml. blood and, on the other hand, according to Paulus and Mallach,[5] it does not pass quantitatively, because on an average only 75% ethylene is regained.

The contact method of Pfeil and Gorbach[6] using catalytic dehydrogenation of ethyl alcohol to acetaldehyde and the determination of acetaldehyde as additional compound with morfolin was not widely applied.

The only nearly specific method is the fermentative one.[7] It uses the catalytic fermentative oxidation of ethanol to aldehyde by alcohol dehydrogenase (ADH) in a buffered solution in the presence of diphosphor pyridin nucleoides (DPH) as hydrogen acceptor (DPN-H). The increase of amount of DPN-H is observed in ultraviolet light at 340 and 366 mμ. In our country, however, the introduction of this method is rather difficult, as DPN and ADH are expensive, their import encounters difficulties and the life of the enzyme reagents is relatively short.

In the present paper the possibility of using gas chromatography (GC)[8, 9] for rapid and specific determinations of alcohol in blood is shown. (A previous report was made at the 4 May Conference of Forensic Physicians in Bratislava). By applying gas chromatography, relatively easy determinations of alcohol in the presence of other volatile substances are possible. GC will surely play an important role in the analytical investigations of biochemical processes and in chemical investigations. As may be seen in the present development of GC, the first experiments to determine alcohol in blood by this method have already been reported.[10, 11] Both methods, however, require a 3–5 ml. sample of blood, from which alcohol is distilled[10] or extracted;[11] and then determined by chromatography. The sensitivity of the method is about 0.1‰, as reported by the authors.

Using hydrophilic stationary liquids for the chromatographic column, it was possible to avoid preliminary conditioning of the blood. By introducing an internal standard of the volatile substance with known concentration to the blood investigated, the necessity of precise dosing of the sample when putting it in the column was avoided. Now the analysis is based on the injection of about 0.10 ml. (thermal conductivity detection), or 0.02 ml. blood (ionization detection) directly on the prepared chromatographic column on measuring the heights of the chromatographic bands of alcohol and the internal standards and, finally, on realizing the calculations.

By a suitable choice of the column packing it is possible to obtain complete separation not only of alcohols and water, but also of ethyl alcohol from methyl alcohol or other organic volatile compounds of blood.

The achieved sensitivity is 0.1‰, the relative error observed on treating the standard alcohol solutions (E. Merck) was 5% in the range of 0.8 to 1.9‰ alcohol. By preliminary comparison with alcohol determinations according to Widmark values lower by about 8–12% relative (0.15–0.20‰) were obtained.[12]

Experimental Methods and Results

For the measurements an apparatus (Griffin & George, London, type MK II) with conventional connexion was used: source and indication of the carried gas, reference side of the detector, column, measuring side of the detector, outlet. Detector and columns were placed into a circulating-air thermostat. As detectors served direct flow thermal conductivity cells,

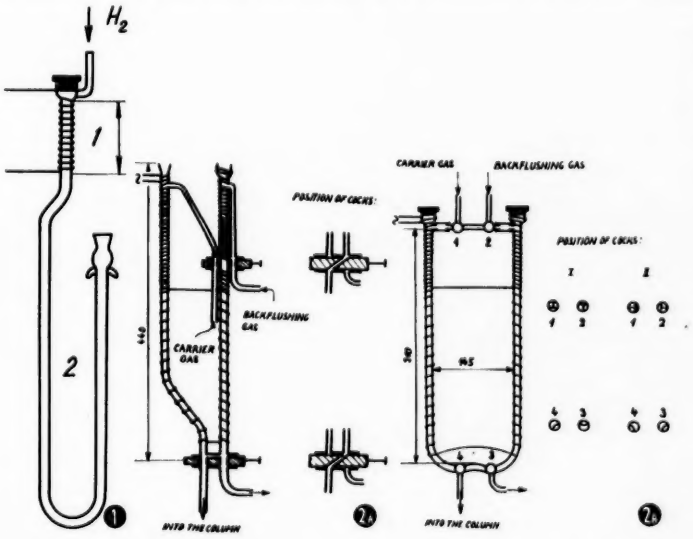
registration was made with a millivoltmeter recorder 0-3 mV Honeywell-Brown. As carrier gas hydrogen from a steel bottle was used, as alcohol samples for calibration served standard solutions from the series 'Alcohol standard solutions', E. Merck, Darmstadt N-butanol containing less than 0.2% of secondary and tertiary butanols as impurities, determined chromatographically. Measurements were also made with the apparatus of 'Laboratorní přístroje', Praha, which is fitted with flame ionization detection, voltage on the electrodes 150 V, with a column in a circulating air thermostat (up to 300°). Carrier gas was nitrogen; additional gas before entering the detector was hydrogen.

The column packing consisted of diglycerol (for GC, May and Baker, London) and carbowax 1500 (polyethylene glycol, Carbide and Carbon Chemicals Co., New York). Sterchamol (Sterchamolwerkw, Dortmund) graining 0.2-0.4 mm., activated 3 hours before at 400°C. was used as carrier. Coating amounted to 25% by weight. Chromatographically pure methyl ethyl ketone served as internal standard.

Determination of the Sum of Alcohols in the Blood

(Thermal Conductivity Detection)

The investigated blood or water solutions of alcohol were prepared by two methods. According to the first method they were injected directly into the modified column (Fig. 1). The upper part of the column (precolumn) was isolated by a glass fibre and heated by a resistance wire to 105–110°C.



(autotransformator regulation) to obtain fastest vaporization of the injected blood samples or water solutions.

The whole column packing amounted to 9.3 g. and of the precolumn to 1.5 g. Sterchamol with 25% diglycerol. The temperature of the thermostat was 100°C., room temperature 24.5°C., hydrogen flow 1.03 ml. per second, speed of the paper 10.0 mm. per minute.

During the preliminary experiments elution intervals of methanol, ethanol, iso- and n-propanol, n-butanol and tertiary butanol acetone and ether were observed. All substances had been distilled before use. In this modification methanol and ethanol are eluted practically in one band which is preceded by the isopropanol and tertiary butanol band and followed by the n-butanol band.

In the second modification of the process we tried to avoid the necessary elution of relatively large quantities of water through the whole column by suitable processing. That could be achieved by refluxing water vapour from the precolumn, the analysis of alcohols passing in the main part of the column. Treatment is illustrated in Figs. 2A, 2B.

Estimation of the Average Error, Measurement of the Conversion Factor and Determination of the Sum of Alcohols in Blood Samples

By a calibrated undivided 1 ml. pipette 1 ml. of the investigated solution (1 ml. water and alcohol standard solution or 1 ml. blood) were precisely measured into a small test tube and exactly 0.25 ml. of an exactly 2% water solution of n-butanol was added from a microburette. The mixture was throughly stirred and about 0.1 ml. of the thus prepared solution was injected by a syringe. As calculation technique the method of measuring heights was chosen, all necessary conditions being kept.[13] As internal standard n-butanol was used following immediately on the chromatogram, but fairly separated from the alcohol, and normally not found in blood. From the relation of the band peaks the conversion factor and after that directly the quantity of ethanol in promille is calculated, following the equation:

$$\text{Ethanol in } {}^{0}/_{00} = \frac{A \cdot V_{Etx}}{V_{Bu} \cdot f} = \frac{5 \cdot V_{Etx}}{V_{Bu5} \cdot f}$$

where 'f' is the factor, corresponding to the relation of the peak heights of ethanol 'V_{Et}' and n-butanol 'V_{Bu}' for equivalent mg. content in the sample, $f = V_{Et}/V_{Bu}$. A is the mg. quantity of n-butanol in the sample, V_{Etx} is the determined peak height of ethanol in the blood sample and V_{Bu5} is the peak height of n-butanol corresponding to 5 mg. n-butanol which were added to the mixture.

In Table I the examination of the average errors of the method when using standard alcohol solutions is reported. It is evident, that the value of

the error of one determination is usually relatively better than 5%; it increases remarkably only if the peak height decreases below 10–15 mm. This is caused by the constant uncertainity of the base line of the record if the measured peak height is decreasing. In practice it is necessary to keep the peak heights of alcohol higher than 10 to 15 mm.

TABLE I

X	V_{Etx}	V_{Bu5}	$V_{Et5}=\frac{V_{Etx5}}{X}$	$f=\frac{V_{Et5}}{V_{Bu5}}$	$X=\frac{5\cdot V_{Etx}}{1{\cdot}538\cdot V_{Bu5}}$	Δ‰
1·90‰	46·5	77·0	122·4	1·590	1·96‰	+0·06
„	26·5	44·2	69·7	1·577	1·95‰	+0·05
1·50‰	26·0	58·0	86·7	1·495	1·46‰	−0·04
„	39·7	88·7	132·3	1·492	1·46‰	−0·04
1·30‰	33·0	81·2	126·9	1·563	1·32‰	+0·02
„	16·8	41·2	64·6	1·568	1·32‰	+0·02
1·10‰	14·0	45·0	63·6	1·413	1·01‰	−0·09
„	32·0	96·5	145·5	1·508	1·08‰	−0·02
0·80‰	6·0	22·0	37·5	1·705	0·89‰	+0·09
„	18·4	78·4	115·0	1·467	0·76‰	−0·04

Average = 1·538

Average error of all determinations ±0·026
Average error of one determination ±0·081

Practical examples of alcohol determinations in blood are illustrated in Table II and compared with the results obtained by Widmark's method. (For the supplied blood samples and analyses by the Widmark method we are indebted to Prof. Dr. O. Wagner, Faculty of Medicine, Brno). The blood samples having been treated 5–8 hours after taking them for ana-

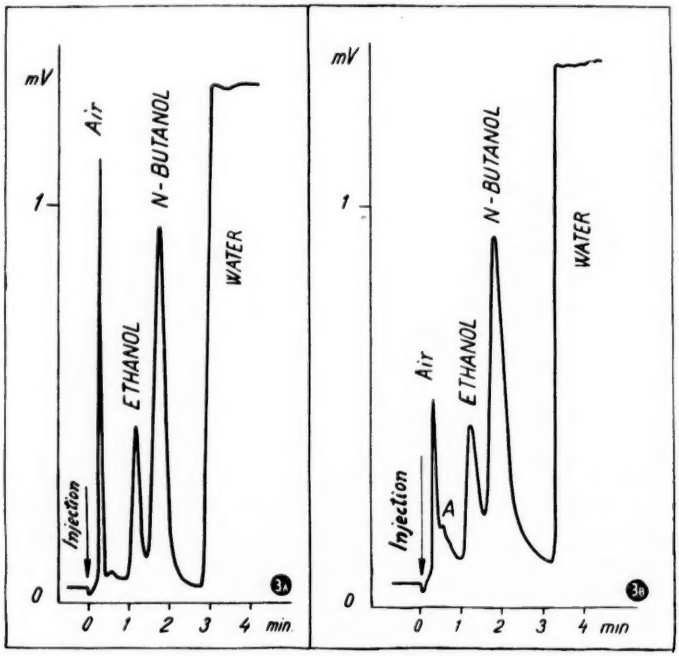
TABLE II

f=1·538

Sample	V_{Etx}	V_{Bu5}	*Determination after Widmark in ‰ (Average of 3 determinations)*	*Found in ‰*	*Absolute Difference in ‰*
1	27·8	42·0		2·15	−0·20
			2·35		
1′	34·6	53·2		2·16	−0·19
2	20·0	58·6		1·11	−0·18
			1·29		
2′	15·0	42·7		1·14	−0·15
3	20·2	48·2		1·36	−0·24
			1·60		
3′	33·9	80·8		1·36	−0·24

lysis according to Widmark from test tubes which had been kept during this time at room temperature and not filled up to the stopper, it is not possible to make precise conclusions as to the large size of the systematic error of Widmark's method.

Figs. 3A and 3B, show the chromatograms of a standard alcohol solution and a blood sample. The chromatographic fraction A (Fig. 3B) is a mixture of volatile substances of non-alcoholic character (hydrocarbons, ketones, aldehydes).



The results of the described analyses are known after 5 minutes, but water elution from the chromatographic column takes about 20–40 minutes. After that the apparatus is ready for another analysis. The alcohol area does positively not include any other volatile substances of non-alcoholic character, but it includes the band of methanol, iso-propanol and tertiary butanol, if they are present. The coated support where in the front part of the column the dry substance of blood is retained, has to be emptied and interchanged for a new one after 15 analyses.

Determination of Ethanol besides Methanol and Other Volatile Substances Pathologically Present in Blood, e.g. Acetone, Formaldehyde, Chlorinated Hydrocarbons (flame ionization detection)

The same principle of sample injection, connected with water removals; allows the use besides diglycerol of also less hydrophilic stationary phases,

e.g. polyethylene glycol. Thus it is possible to obtain separation of methanol from ethanol and n-propanol.

The precolumn packing consisted of 5.8 g. Sterchamol, impregnated by diglycerol and the analytical column packing was 17.8 g. Sterchamol impregnated by polyethylene glycole. The precolumn was heated to the temperature 105–110°C.; the temperature of the analytical column was 60 C. The speed of the carrier gas amounted to 1.4 ml. N_2/s and 0.78 ml. N_2/s; the speed of the added gas 1.0 ml. H_2/s. Two minutes after sample injection the precolumn was dismounted and the water removed by the back-flushing gas (nitrogen). The paper rolled at the speed 13.0 mm. per minute.

Estimation of the Average Error and Determination of the Conversion Factor

In Table III the results of investigating the average error of the method using synthetic water solutions of alcohol and methyl ethyl ketone as internal standard are shown.

TABLE III

Sample	*Concentration of Methyl Ethyl Ketone in* ‰	*Peak Height of Methyl Ethyl Ketone (in mm.)*	*Concentration of Ethanol (in* ‰*)*	*Peak Height of Ethanol (in mm.)*	$f = \frac{\text{MEK in mm} \cdot \text{‰ Et}}{\text{Et in mm} \cdot \text{‰ MEK}}$
1	0·4	50	2·0	123	2·03
1′	0·4	54	2·0	140	1·93
2	0·4	54·5	1·6	115	1·89
3	0·4	43·5	1·2	64	2·04
4	0·4	33·5	0·8	33	2·03
5	0·4	132·0	0·4	61	2·16
5′	0·4	41	0·4	19	2·16
6	0·4	61·5	1·0	78	1·97
3′	0·4	50	1·6	75	2·00
5′	0·4	46	0·4	22·5	2·04

Average error of all determinations = 1·996 + 0·085

The value of the error of one determination is almost the same as with the thermal conductivity alternative.

Some examples of alcohol determinations in blood are given in Table IV.

Fig. 4A shows the chromatogram of a synthetic water solution containing ether (1), formaldehyde (2), acetone (3), methyl ethyl ketone (4), methyl alcohol (5) and ethyl alcohol (6) in such concentrations as may be found in pathological blood.

Fig. 4B is the chromatogram of the blood of the deceased M.W., aged 33 (Diagnosis: Ethylismus chronicus, steatosis hepatis diffusa gravis,

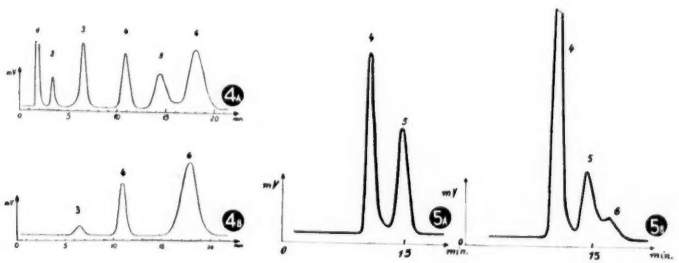
aspiratio terminalis vomitus, oedema cerebri et pulmonum, cyanosis peripherica) where, besides ethyl alcohol, the presence of a considerable quantity of acetone was found.

The same was found in the distillate of the stomach contents.

TABLE IV

Sample	*Peak Height of Ethanol (in mm.)*	*Peak Height of Methyl Ethyl Ketone (in mm.)*	*Average of 3 determinations after Widmark (in ‰)*	*Found (in ‰)*	*Average Value (in ‰)*	*Absolute Difference (in ‰)*
T.	5·0	51·0	0·15‰	0·196	0·16	+ 0·01
	12·2	199·5		0·122		
D.	149·0	119·5	2·25‰	2·52	2·53	+ 0·28
	157·5	124·0		2·54		
N.J.	118·0	158·0	1·50‰	1·49	1·48	− 0·02
	68·5	94·0		1·46		
59/59	67·0	64·0	2·02‰	1·94	2·01	− 0·01
	83·5	80		2·09		

Fig. 5A is the chromatogram of a mixture of methanol (5) with methyl ethyl ketone (4) as internal standard and Fig. 5B a chromatogram of the blood of J.K., who died of methanol poisoning.



We continue our studies by statistical comparisons of the results obtained by the Widmark method and of the results achieved by GC and, on the other hand, by further elaboration of rapid and specific evidence of other volatile substances in biological material.

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Abstracts

Psycho-Active Drugs and Handwriting

Pharmacographological effects fall into a few basic patterns: graphomotor activation, relaxation, inhibition and abolition. These basic patterns can be ascribed to pharmacological effects involving the interplay of impulse, inhibition and control in the psychomotor processes of writing. Various psycho-active drugs may provoke the same effects: one and the same preparation is capable, depending on its dosage level and the individual basic psychomotor state of the writer, of inducing different effects.

During courses of treatment with large doses of Serpasil or chlorpromazine, graphomotor inhibition can be observed. Sometimes, the handwriting shrinks to the level of micrography. Writing speed is, on the whole, appreciably reduced, and the pen strokes are unsteady. The patient no longer has the necessary control for small, precise forms. Coordination is inaccurate. Writing pressure is often reduced as a sign of the diminution in motor activity. The stiffness of movement is presumably chiefly primary (i.e. not reactive), especially as the motor effects of Serpasil and chlorpromazine are not necessarily associated with a feeling of fatigue. It is interesting to note that the damping down of the motor centre is usually accompanied by a loss of psychic activity, which is reflected by a lack of drive and a diminution in initiative and interest.

[Grünewald, G. (1959): Arch. Psychiatr. u. Zschr. Neurol., **198**, 687.]

Hypertension and Vestibular Function

The efficiency of the vestibule was tested in 40 hypertensives who showed not the slightest signs of any clinically demonstrable neurological deficiency. More than half the patients, however, complained of subjective phenomena which could only be ascribed to dysfunction of the vestibular apparatus. The symptoms looked for included giddiness, disturbed sense of balance and nystagmus.

Vestibular symptoms were objectively demonstrated in 36 of the 40 hypertensives. This result tallies with the findings of Solomonof, who made the same observation in 83% of 128 patients. Our present knowledge of the subject does not entitle us to assert that there is a symptomatology of vestibular disorders which can be regarded as typical of the hypertensive

patient; nor is there any correlation between the blood pressure level on the one hand and the extent and location of the vestibular disorder on the other.

Apparently, the circulatory changes which occur in hypertension affect the efficiency of the vestibular apparatus in varying degrees and at different points. Where the patient complains of subjective disorders, it is almost always possible to find objective evidence of changes in the vestibular reflexes.

[Borri, G. and C. Marobbio (1959): Minerva Med., **50**, 1977].

Psychoses and the Pneumo-Encephalogram

Nagy conducted pneumo-encephalographic studies in 479 mental patients with the aim of seeking answers to four questions. The first was: are the changes in the pneumo-encephalogram (PEG) specific for a particular psychosis? It was found that, although atrophic cerebral changes were present in schizophrenia, depression, and psychogenic psychoses, these findings were not specific for a particular type of mental disease; however, the incidence of the alterations varied in the different groups of diseases.

The second question—whether there is any connection between pneumo-encephalographic changes and age—was answered as follows: the incidence of abnormal findings rises from decade to decade. It can be assumed that a continuous physiological process of degeneration and involution begins in the brain in the third or fourth decade, though the speed of the process varies.

The third question was: are there any connections between the duration of the disease and the PEG changes? It may be regarded as very probable that a lengthy mental illness (schizophrenia at least) causes modifications in the nerve substance for which objective evidence can be found in the PEG.

The fourth question—whether there are regular connections between personality defects and PEG—must be answered in the negative.

[Nagy, K. (1959): Arch. Psychiatr. u. Zschr. Neurol., **198**, 544].

Ganglion Blockers in Cerebral Trauma

Ganglion blockers are frequently indicated in cases of cerebral trauma, since they reduce the cerebral oedema and inhibit the formation of cerebrospinal fluid. The results are particularly good in contusion of the brain and concussion, as well as in subarachnoid haemorrhages which do not require surgery.

[Raduschkewitsch, W. P. (1959): Zbl. Chir., **84**, 708].

Book Review

Hysterical Amnesia

Crime Documentaries: Guenther Podola. By Rupert Furneaux. (1960. Pp. 319. With Figs. 18s. 6d.). London: Stevens & Sons Limited.

This is the first volume in a series of crime documentaries. Mr. Furneaux has edited a detailed account of the Podola trial in a manner which makes the record a matter of considerable professional interest to legal as well as medical practitioners.

It will be recalled that Podola was tried and convicted of capital murder for the shooting of a policeman. He based his defence of inability to plead on an alleged hysterical amnesia, a plea apparently unique in English criminal law.

The legal reader will be instructed as well as entertained by the adept cross-examination of the medical experts. Close scrutiny of the technique of cross-examination of the psychiatric experts would also be a useful exercise for potential medical witnesses. In no other branch of medicine does there seem to be such a diversity of views which medical practitioners are capable of holding on the same facts. In the course of the Podola trial medical experts went through the whole gamut of possible opinion about the genuineness of the accused's amnesia. They ranged from the cautious to the utterly dogmatic—a state of affairs which does not necessarily enhance the status of expert medical testimony.

The volume is an interesting 'first' in a new series. Its excellent preparation augurs well for those which will follow it.